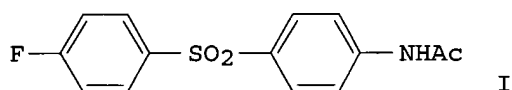
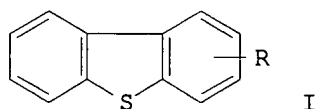


ACCESSION NUMBER: 1987:310 HCAPLUS
 DOCUMENT NUMBER: 106:310
 TITLE: Immunoprotective and immunorestorative effects of a
 new immunomodulator, CL 259,763
 AUTHOR(S): Durr, F. E.; Wallace, R. E.; Ruzsala-Mallon, V.; Wang,
 B. S.
 CORPORATE SOURCE: Med. Res. Div., American Cyanamid Co., Pearl River,
 NY, USA
 SOURCE: Recent Adv. Chemother., Proc. Int. Congr. Chemother.,
 14th (1985), Volume Anticancer Sect. 2, 922-3.
 Editor(s): Ishigami, Joji. Univ. Tokyo Press: Tokyo,
 Japan.
 CODEN: 55GNAX
 DOCUMENT TYPE: Conference
 LANGUAGE: English
 GI



- AB CL 259763 (I) [734-22-5] is an orally active compd. that affects the
 humoral and cellular compartments of the immune system in both normal and
 tumor-bearing mice. I potentiates the antibody response to sheep
 erythrocytes in normal mice, restores the antibody response in
 immunosuppressed leukemic mice, and protects the humoral response from
 suppression by cytotoxic drugs. I also protects or accelerates the
 recovery of bone marrow following myelosuppression by cytotoxic drugs, an
 effect possibly mediated by colony-stimulating factor [62683-29-8], which
 is induced by the compd.
- IT Neoplasm inhibitors
 (myelosuppression from, CL 259763 protection against)
- IT Immunosuppression
 (treatment of, with CL 259763)
- IT Immunostimulants
 (adjuvants, CL 259763 as, cytotoxic drug-induced myelosuppression
 prevention by)
- IT Hematopoiesis
 (myelopoiesis, suppression of, by cytotoxic agents, CL 259763
 protection from)
- IT 734-22-5, CL 259763
 RL: BIOL (Biological study)
 (immunomodulation by, cytotoxic drug-induced myelosuppression response
 in relation to)
- IT 62683-29-8
 RL: BIOL (Biological study)
 (in CL 259763 immunomodulation effects)
- IT 65271-80-9, Mitoxantrone
 RL: BIOL (Biological study)
 (myelosuppression from, [[(fluorophenyl)sulfonyl]phenyl]acetamide
 protection from)

ACCESSION NUMBER: 1993:254663 HCAPLUS
 DOCUMENT NUMBER: 118:254663
 TITLE: Sulfur compounds from petroleum. XVI.
 Dibenzothiophenes with linear C1-C5 alkyl side chains
 AUTHOR(S): Boberg, Friedrich; Bruns, Wolfgang; Musshoff, Dagmar
 CORPORATE SOURCE: Inst. Org. Chem., Tech. Univ. Clausthal,
 Clausthal-Zellerfeld, D-3392, Germany
 SOURCE: Phosphorus, Sulfur Silicon Relat. Elem. (1992),
 72(1-4), 13-31
 CODEN: PSSLEC; ISSN: 1042-6507
 DOCUMENT TYPE: Journal
 LANGUAGE: German
 OTHER SOURCE(S): CASREACT 118:254663
 GI



AB The prepn. of all position isomers of dibenzothiophenes I [e.g., R = Me, Et, Pr, Bu, C(O)R] with a linear C1-C5-sidechain and of the corresponding 5,5-dioxides is described. E.g., Friedel-Crafts acylation of I (R = H) with RCOCl (e.g., R = Bu) in dry CS₂ and AlCl₃ gave I [R = 2-C(O)Bu] (II) in 48% yield and I [R = 4-C(O)Bu] in 15% yield. II underwent Huang-Minlon redn. by N₂H₂/KOH to give I (R = 2-Bu). ¹H NMR data and GC-purities are given.

IT **127330-24-9P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and Huang-Minlon redn. of, with hydrazine)

IT Friedel-Crafts reaction
 (of dibenzothiophenes)

IT Reduction
 (Huang-Minlon, of acyldibenzothiophene, alkyldibenzothiophenes from)

IT 75-36-5, Acetyl chloride 79-03-8, Propanoyl chloride 141-75-3,
 Butanoyl chloride 638-29-9, Pentanoyl chloride
 RL: RCT (Reactant)

(Friedel-Crafts acylation by, of dibenzothiophene deriv.)

IT 132-65-0, Dibenzothiophene 16587-33-0
 RL: RCT (Reactant)

(Friedel-Crafts acylation of)

IT 22439-58-3P **127330-24-9P** 147792-12-9P 147792-13-0P
 147792-14-1P 147792-15-2P 147792-20-9P 147792-21-0P 147792-22-1P
 147792-23-2P 147792-24-3P 147792-25-4P 147792-26-5P 147792-27-6P
 147792-28-7P 147792-29-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and Huang-Minlon redn. of, with hydrazine)

IT 31317-07-4P 89816-97-7P 147792-09-4P 147792-10-7P 147792-11-8P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)

(prepn. and oxidn. of, dibenzothiophene dioxide deriv. from)

IT 7372-88-5P 16587-52-3P 20928-02-3P 89816-98-8P 89816-99-9P
 89817-03-8P 97193-85-6P 132034-86-7P 147792-30-1P 147792-31-2P
 147792-32-3P 147792-33-4P 147792-34-5P 147792-45-8P 147792-46-9P
 147792-47-0P 147792-52-7P 147792-53-8P 147792-54-9P

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. and peroxide-oxidn. of, dibenzothiophene dioxide deriv. from)

IT 34724-69-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)

(prepn. and redn. of)

IT 20928-03-4P 23657-53-6P 113222-81-4P 113222-82-5P 147792-16-3P
 147792-17-4P 147792-18-5P 147792-19-6P 147792-35-6P 147792-36-7P
 147792-37-8P 147792-38-9P 147792-39-0P 147792-40-3P 147792-41-4P
 147792-42-5P 147792-43-6P 147792-44-7P 147792-48-1P 147792-49-2P
 147792-50-5P 147792-51-6P 147792-58-3P 147792-59-4P 147792-60-7P
 147792-61-8P 147792-62-9P 147792-63-0P 147792-64-1P 147792-65-2P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of)

IT 96749-91-6P 147792-55-0P 147792-56-1P 147792-57-2P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn., peroxide-oxidn. and o-chloranil-dehydrogenation of,
 alkyldibenzothiophene from)

IT 34724-68-0, 1-Dibenzothiophenecarboxylic acid
 RL: RCT (Reactant)
 (reductive alkylation of)

IT 22439-61-8 97511-04-1
 RL: RCT (Reactant)
 (sequential lithiation and reaction of, with dialkyl sulfate)

L6 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1990:515068 HCAPLUS

DOCUMENT NUMBER: 113:115068

TITLE: Preparation of dibenzothiophenes as hematocyte
 regeneration stimulants

PATENT ASSIGNEE(S): American Cyanamid Co., USA

SOURCE: Jpn. Kokai Tokkyo Koho, 36 pp.

CODEN: JKXXAF

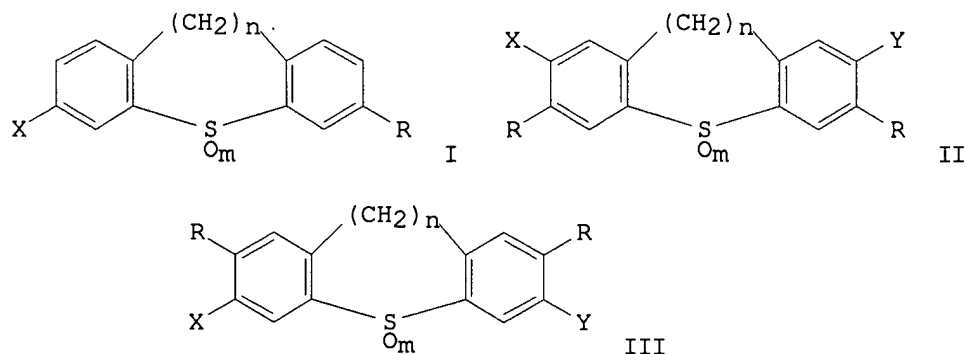
DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 02017184	A2	19900122	JP 1989-124639	19890519
US 4965284	A	19901023	US 1989-341862	19890425
PRIORITY APPLN. INFO.:			US 1988-196166	19880519
			US 1989-341862	19890425
OTHER SOURCE(S):		MARPAT 113:115068		
GI				



AB The title compds. I, II, and III [Y, X = H, F, Cl, Br; n = 0 or 1; m = 0-2; R = N:CR₁NR₂R₃, NR₅COR₄, etc.; R₁ = alkyl, cycloalkyl, (substituted) Ph, pyridine, etc.; R₂ = H, alkyl, PhCH₂; R₃ = alkyl, cycloalkyl; R₄ = alkyl, (substituted) Ph, CH₂COMe, CH₂NMe₂; R₅ = H, alkyl; R₁R₂ may form

(CH₂)_q; q = 2-5; or NR₂R₃ = pyrrolidino, morpholino, thiomorpholino, 4-methylpiperidino, etc.], were prepd. A mixt. of 7-fluoro-3-dibenzothiopheneamine S,S-dioxide and Ac₂O in pyridine was set aside for 1.5 h to give N-(7-fluoro-3-dibenzothiophenyl)acetamide S,S-dioxide (IV). IV at 100 mg/kg increased the generation of interleukin-2 in mice by 30%.

IT **127330-50-1P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, in prepn. of drug)

IT **127330-19-2P 127330-20-5P 127330-21-6P**

127330-40-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, in prepn. of hematocyte regeneration
stimulant)

IT **127330-36-3P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

IT **127330-22-7P 127330-23-8P 127330-42-1P**

127330-43-2P 127330-45-4P 127330-46-5P

127330-48-7P 127330-66-9P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as hematocyte regeneration stimulant)

IT **127330-50-1**

RL: RCT (Reactant)
(reaction of, in prepn. of hematocyte regeneration stimulant)

IT Immunostimulants

(dibenzothiophenes)

IT Leukocyte

(precursors of, dibenzothiophenes effect on)

IT 1199-51-5P 14313-93-0P **127330-50-1P** 128142-08-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, in prepn. of drug)

IT 1696-17-9P, N,n-Diethylbenzamide 6259-19-4P 22439-58-3P 35105-75-0P
35105-81-8P 50863-19-9P 51762-59-5P 93618-98-5P 95200-70-7P

127330-19-2P 127330-20-5P 127330-21-6P

127330-40-9P 128142-04-1P 128142-05-2P 128142-06-3P
128169-36-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, in prepn. of hematocyte regeneration
stimulant)

IT **127330-36-3P** 128141-91-3P 128141-92-4P 128141-93-5P

128141-94-6P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

IT 54635-78-8P **127330-22-7P 127330-23-8P**

127330-42-1P 127330-43-2P 127330-45-4P

127330-46-5P 127330-48-7P 127330-66-9P

128141-87-7P 128141-88-8P 128141-89-9P 128141-90-2P 128141-95-7P

128141-96-8P 128141-97-9P 128141-98-0P 128141-99-1P 128142-00-7P

128142-01-8P 128142-02-9P 128169-34-6P 128169-35-7P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as hematocyte regeneration stimulant)

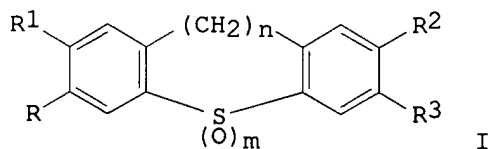
IT 79-16-3 80-73-9 127-19-5 132-65-0, Dibenzothiophene 134-62-3,
N,N-Diethyl-m-toluamide 283-24-9, 3-Azabicyclo[3,2,2]nonane 503-29-7,
Azetidine 685-91-6, N,N-Diethylacetamide 758-96-3,
N,N-Dimethylpropionamide 931-20-4 1016-05-3, Dibenzothiophenesulfone
1114-51-8, N,N-Diethylpropionamide 1119-49-9 2403-22-7,
N-Benzylbutylamine 5006-22-4, Cyclobutylcarbonyl chloride 5271-67-0,
2-Thiophenecarbonyl chloride 6259-19-4 6837-24-7, 1-Cyclohexyl-2-
pyrrolidinone 7428-91-3, 2-Aminodibenzothiophene 10215-25-5
14313-93-0 23863-19-6 35105-75-0, 2,8-Diacetyldibenzothiophene
39098-97-0, 2-Thiopheneacetyl chloride 41738-64-1, 3,7-
Dibenzothiophenediamine 50863-19-9 58920-49-3, 3,7-

Dinitrobenzothiophene S,S-dioxide 78769-83-2, 2,8-
 Dibenzothiophenediamine 95200-70-7 **127330-50-1** 128142-03-0
 128142-09-6, 9H-Thioxanthene-3,6-diamine
 RL: RCT (Reactant)
 (reaction of, in prepn. of hematocyte regeneration stimulant)

L6 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1990:235168 HCAPLUS
 DOCUMENT NUMBER: 112:235168
 TITLE: Preparation of substituted dibenzothiophenes as
 immunomodulators and antitumor agents
 INVENTOR(S): Nair, Vijay Gopalan; Conrow, Ransom Brown; Wang, Bosco
 Shang; Ruszala-Mallon, Veronica M.
 PATENT ASSIGNEE(S): American Cyanamid Co., USA
 SOURCE: Eur. Pat. Appl., 39 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 342433	A2	19891123	EP 1989-107997	19890503
EP 342433	A3	19910619		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, NL, SE				
DK 8902417	A	19891120	DK 1989-2417	19890518
NO 8901985	A	19891120	NO 1989-1985	19890518
FI 8902398	A	19891120	FI 1989-2398	19890518
AU 8934911	A1	19891207	AU 1989-34911	19890518
ZA 8903738	A	19900131	ZA 1989-3738	19890518
DD 283819	A5	19901024	DD 1989-328702	19890518
PRIORITY APPLN. INFO.:			US 1988-196166	19880519
OTHER SOURCE(S):	MARPAT 112:235168			
GI				



AB Title compds. I [R-R3 = H, Br, Cl, F, EtOCH:N, substituted aminomethyleneamino, substituted carbamoyl, [(1,3-dimethyl-2-imidazolidinylidene)amino]; m = 0-2; n = 0, 1] and their pharmaceutically acceptable salts, were prepd. Significant activity of I in each aspect was examd. for their immunomodulatory activity (assay for macrophage-mediated tumor cystostasis, prodn. of interleukins, anti-sheep red blood cell antibody assay, colony-forming factor prodn. and assay to measure acceleration of myeloid cell recovery following 5-fluorouracil therapy). I (R = F, R1 = R2 = H, R3 = MeCONH) showed significant activity in all the above assays.

IT **127330-18-1P 127330-19-2P 127330-20-5P**
127330-21-6P 127330-24-9P 127330-25-0P
127330-26-1P 127330-27-2P 127330-29-4P
127330-31-8P 127330-34-1P 127330-41-0P
127330-50-1P 127343-46-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, in prepn. of antitumor and immunostimulant agents)

IT 127330-16-9P 127330-22-7P 127330-23-8P
127330-28-3P 127330-30-7P 127330-32-9P
127330-33-0P 127330-35-2P 127330-36-3P
127330-37-4P 127330-38-5P 127330-39-6P
127330-40-9P 127330-42-1P 127330-43-2P
127330-44-3P 127330-45-4P 127330-46-5P
127330-47-6P 127330-48-7P 127330-49-8P
127330-51-2P 127330-52-3P 127330-53-4P
127330-54-5P 127330-55-6P 127330-56-7P
127330-57-8P 127330-58-9P 127330-59-0P
127330-60-3P 127330-61-4P 127330-62-5P
127330-63-6P 127330-64-7P 127330-65-8P
127343-47-9P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as antitumor and immunostimulant)

IT 127330-66-9

RL: RCT (Reactant)

(reaction of, in prepn. of antitumor and immunostimulant agents)

IT Immunostimulants

Neoplasm inhibitors

(substituted dibenzothiophenes)

IT 132-65-0, Dibenzothiophene 180-44-9, 3-Azaspiro[5.5]undecane 283-24-9,
3-Azabicyclo[3.2.2]nonane 503-29-7, Azetidine

RL: RCT (Reactant)

(acetylation of)

IT 123-90-0, Thiomorpholine

RL: RCT (Reactant)

(amidation by, of cyclobutanecarbonyl chloride)

IT 2403-22-7, N-Benzylbutylamine

RL: RCT (Reactant)

(amidation by, of isovaleryl chloride)

IT 108-12-3, Isovaleryl chloride

RL: RCT (Reactant)

(amidation of, with benzylbutylamine)

IT 79-04-9, Chloroacetyl chloride

RL: RCT (Reactant)

(amidation of, with diaminodibenzothiophene dioxide)

IT 98-88-4, Benzoyl chloride 5271-67-0, 2-Thiophenecarbonyl chloride
39098-97-0, 2-Thiopheneacetyl chloride

RL: RCT (Reactant)

(amidation of, with diethylamine)

IT 5006-22-4, Cyclobutanecarbonyl chloride

RL: RCT (Reactant)

(amidation of, with thiomorpholine)

IT 1199-51-5P 1696-17-9P 6259-19-4P 14313-93-0P 23863-19-6P
45467-31-0P 51762-59-5P 58920-49-3P 93618-98-5P 95200-70-7P

127330-18-1P 127330-19-2P 127330-20-5P

127330-21-6P 127330-24-9P 127330-25-0P

127330-26-1P 127330-27-2P 127330-29-4P

127330-31-8P 127330-34-1P 127330-41-0P

127330-50-1P 127343-46-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)

(prepn. and reaction of, in prepn. of antitumor and immunostimulant agents)

IT 127330-16-9P 127330-22-7P 127330-23-8P

127330-28-3P 127330-30-7P 127330-32-9P

127330-33-0P 127330-35-2P 127330-36-3P

127330-37-4P 127330-38-5P 127330-39-6P

127330-40-9P 127330-42-1P 127330-43-2P

127330-44-3P 127330-45-4P 127330-46-5P
127330-47-6P 127330-48-7P 127330-49-8P
127330-51-2P 127330-52-3P 127330-53-4P
127330-54-5P 127330-55-6P 127330-56-7P
127330-57-8P 127330-58-9P 127330-59-0P
127330-60-3P 127330-61-4P 127330-62-5P
127330-63-6P 127330-64-7P 127330-65-8P
127343-47-9P

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of, as antitumor and immunostimulant)

IT 122-51-0 685-91-6 758-96-3 872-50-4, 1-Methyl-2-pyrrolidinone,
reactions 1016-05-3, Dibenzothiophene sulfone 1114-51-8,
Diethylpropionamide 1696-20-4, N-Acetylmorpholine 4637-24-5
7428-91-3, 2-Aminodibenzothiophene 10215-25-5, 3,6-Thioxanthenediamine
10,10-dioxide 95200-70-7 **127330-66-9**

RL: RCT (Reactant)

(reaction of, in prepn. of antitumor and immunostimulant agents)

=>

L3 ANSWER 1 OF 1 USPATFULL

ACCESSION NUMBER: 90:81811 USPATFULL
TITLE: Substituted dibenzothiophenes
INVENTOR(S): Nair, Vijay G., Nanuet, NY, United States
Conrow, Ramson B., Pearl River, NY, United States
Wang, Bosco S., Cranbury, NY, United States
Ruszczyk-Mallon, V. M., New City, NY, United States
PATENT ASSIGNEE(S): American Cyanamid Company, Wayne, NJ, United States
(U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 4965284		19901023	<--
APPLICATION INFO.:	US 1989-341862		19890425	(7)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1988-196166, filed on 19 May 1988, now abandoned			
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Ford, John M.			
ASSISTANT EXAMINER:	Scalzo, Catherine			
LEGAL REPRESENTATIVE:	Dow, Kenneth J.			
NUMBER OF CLAIMS:	23			
EXEMPLARY CLAIM:	1			
NUMBER OF DRAWINGS:	2 Drawing Figure(s); 2 Drawing Page(s)			
LINE COUNT:	1219			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This disclosure described novel derivatives of dibenzothiophene, dibenzothiophene sulfoxide, dibenzothiophene sulfone, thioxanthene, thioxanthene sulfoxide and thioxanthene sulfone which are active as modulators of the mammalian immune response system.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT Immunostimulants
IT Neoplasm inhibitors
(substituted dibenzothiophenes)
IT 132-65-0, Dibenzothiophene 180-44-9, 3-Azaspiro[5.5]undecane
283-24-9, 3-Azabicyclo[3.2.2]nonane 503-29-7, Azetidine
(acetylation of)
IT 123-90-0, Thiomorpholine
(amidation by, of cyclobutanecarbonyl chloride)
IT 2403-22-7, N-Benzylbutylamine
(amidation by, of isovaleryl chloride)
IT 108-12-3, Isovaleryl chloride
(amidation of, with benzylbutylamine)
IT 79-04-9, Chloroacetyl chloride
(amidation of, with diaminodibenzothiophene dioxide)
IT 98-88-4, Benzoyl chloride 5271-67-0, 2-Thiophenecarbonyl chloride
39098-97-0, 2-Thiopheneacetyl chloride
(amidation of, with diethylamine)
IT 5006-22-4, Cyclobutanecarbonyl chloride
(amidation of, with thiomorpholine)
IT 1199-51-5P 1696-17-9P 6259-19-4P 14313-93-0P 23863-19-6P
45467-31-0P 51762-59-5P 58920-49-3P 93618-98-5P 95200-70-7P
127330-18-1P 127330-19-2P 127330-20-5P 127330-21-6P 127330-24-9P
127330-25-0P 127330-26-1P 127330-27-2P 127330-29-4P 127330-31-8P
127330-34-1P 127330-41-0P 127330-50-1P 127343-46-8P
(prepn. and reaction of, in prepn. of antitumor and immunostimulant agents)
IT 127330-16-9P 127330-22-7P 127330-23-8P 127330-28-3P 127330-30-7P
127330-32-9P 127330-33-0P 127330-35-2P 127330-36-3P 127330-37-4P
127330-38-5P 127330-39-6P 127330-40-9P 127330-42-1P 127330-43-2P
127330-44-3P 127330-45-4P 127330-46-5P 127330-47-6P 127330-48-7P

127330-49-8P 127330-51-2P 127330-52-3P 127330-53-4P 127330-54-5P
127330-55-6P 127330-56-7P 127330-57-8P 127330-58-9P 127330-59-0P
127330-60-3P 127330-61-4P 127330-62-5P 127330-63-6P 127330-64-7P
127330-65-8P 127343-47-9P

(prepn. of, as antitumor and immunostimulant)

IT 122-51-0 685-91-6 758-96-3 872-50-4, 1-Methyl-2-pyrrolidinone,
reactions 1016-05-3, Dibenzothiophene sulfone 1114-51-8,
Diethylpropionamide 1696-20-4, N-Acetylmorpholine 4637-24-5
7428-91-3, 2-Aminodibenzothiophene 10215-25-5, 3,6-Thioxanthenediamine
10,10-dioxide 95200-70-7 127330-66-9

(reaction of, in prepn. of antitumor and immunostimulant agents)

=>

L6 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1990:210715 CAPLUS

DOCUMENT NUMBER: 112:210715

TITLE: Generation of tumoricidal effector **cells**
with a novel potentiator: N-[4-[(4-
fluorophenyl)sulfonyl]phenyl]acetamide (CL 259,763).
AUTHOR(S): Wang, Bosco Shang; Lumanglas, Araceli L.; Lin, Yang
I.; Durr, Frederick E.

CORPORATE SOURCE: Med. Res. Div., Am. Cyanamid Co., Pearl River, NY,
10965, USA

SOURCE: International Journal of Immunopharmacology (1990),
12(3), 307-14

CODEN: IJIMDS; ISSN: 0192-0561

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The effects of the title immunopotentiator on the generation of
tumoricidal effector **cells** were studied. A single oral dose of
the compd. (100-600 mg/kg) induced in mice a population of peritoneal
macrophages capable of inhibiting the growth of tumor **cells**.
These activated macrophages released proteases which seemed responsible
for the tumor **cell** inhibition, because the cytostatic activity
was abrogated in the presence of protease inhibitors, on the other hand,
addn. of catalase and arginine to the culture failed to alter the effect,
suggesting that H2O2 and arginase did not participate in this system.
Although induction of cytolytic T-lymphocytes (CTL) reactive with
syngeneic tumor **cells** was achievable in mice previously
sensitized to the tumor, treatment with CL 259,763 rendered these animals
even more response to tumor antigens, resulting in enhancement of tumor
cell destruction. The compd. was effective in augmenting the CTL
response over a rather broad dose range of 25-200 mg/kg. In contrast to
these stimulatory effects, the cytolytic activity of natural killer
cells seemed to be affected by the compd. Thus, CL 259,763 is an
orally active immunomodulator capable of inducing tumor-inhibitory
macrophages and potentiating CTL responses to syngeneic tumor
cells; therefore, it may prove clin. useful in the treatment of
neoplastic diseases.

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ARTICLES

Restoration of cytolytic T-lymphocyte response with a new immunopotentiator, N-(4-[(4-fluorophenyl)sulfonyl]phenyl)acetamide (CL 259, 763), in mice

BS Wang, VM Ruzsala-Mallon, AL Lumanglas, J Silva and FE Durr

Chemotherapy Research Department, American Cyanamid Company, Lederle Laboratories, Pearl River, New York 10965.

The immunorestorative characteristics of a novel synthetic immunomodulator, N-(4-[(4-fluorophenyl)sulfonyl]phenyl)acetamide (CL 259, 763), has been investigated in several experimental models. In one situation, the compound was shown to enhance the induction of a cytolytic T-lymphocyte response to the murine MBL-2 leukemia implanted in its syngeneic host in which only a minimal reactivity to the tumor is normally displayed. In a Vaccinia virus model, the compound similarly augmented the lytic activity of cytolytic T-lymphocyte to virus-infected targets in not only viral antigen-primed but also cyclosporin A-impaired mice. Likewise, the alloreactive cytolytic T-lymphocyte activity was recovered in animals immunocompromised by inoculation with murine plasmacytomas or cytoreductive anticancer drugs, such as cyclophosphamide and 5-fluorouracil. Thus, the present findings suggest that CL 259,763 is effective in potentiating the immune response to weak antigens as well as in restoring alloreactivity by sparing the immunotoxicity associated with the administration of cytotoxic drugs and the growth of neoplasms.

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